

What Is Claimed Is:

1. A molecule comprising a DNA sequence encoding a polypeptide which is capable of binding to RIP and modulating or mediating the intracellular activity of RIP, which polypeptide is:

(a) a RIP-associated protein (RAP) encoded by said DNA sequence in a clone deposited with collection Nationale de Cultures de Microorganisme under the accession number I-2706;

(b) a fragment of (a) which is capable of binding to RIP or inhibiting the NF- $\kappa$ B inducing effect of RIP; or

(c) an analog of (a) or (b) which differs from the sequence of (a) or (b) by no more than 10 substitutions, deletions and/or insertions of amino acid residues and is capable of binding to RIP or inhibiting the NF- $\kappa$ B inducing effect of RIP.

2. A molecule according to claim 1, wherein said DNA sequence encodes a RAP protein having the amino acid sequence of SEQ ID NO:2.

3. A molecule according to claim 1, comprising the sequence of SEQ ID NO:1.

4. A molecule in accordance with claim 1, wherein said DNA sequence is:

(i) the cDNA sequence of SEQ ID NO:1; or

(ii) a DNA sequence which encodes the amino acid sequence encoded by the DNA sequence of (i).

5. A molecule in accordance with claim 1 which is a vector.

6. A vector according to claim 5 capable of expressing the polypeptide encoded therein in a eukaryotic host cell.

7. A vector according to claim 5 capable of expressing the polypeptide encoded therein in a prokaryotic host cell.

8. Transformed eukaryotic or prokaryotic host cells containing a vector according to claim 5.

9. A method for producing a polypeptide capable of binding to RIP and modulating or mediating the intracellular activity of RIP, comprising growing the transformed host cells according to claim 8 under conditions suitable for the expression of said polypeptide, effecting post-translational modifications as necessary for obtaining said polypeptide and isolating said expressed polypeptide.

10. A pharmaceutical composition for modulating the RIP effect on cells, comprising, as active ingredient, an oligonucleotide sequence encoding an anti-sense sequence of the DNA sequence according to claim 1.

11. A method for modulating the RIP modulated/mediated effect on cells, comprising treating said cells with an oligonucleotide sequence encoding an antisense sequence for at least part of the DNA sequence encoding a RAP protein according to claim 1; said oligonucleotide sequence being capable of blocking the expression of the RAP protein.

12. A method according to claim 11, wherein said oligonucleotide sequence is introduced to said cells by transfection of said cells with a recombinant animal virus vector comprising:

(a) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein (ligand) that is capable of binding to a specific cell surface receptor on the surface of said cells to be treated and a second sequence encoding said oligonucleotide sequence; and

(b) infecting said cells with said vector of (a).

13. An isolated polypeptide which is capable of binding to RIP and modulating or mediating the intracellular activity of RIP, which polypeptide is:

(a) a RIP-associated protein (RAP) encoded by a DNA sequence in a clone deposited with Collection Nationale de Cultures de Microorganismes under accession number I-2706;

(b) a fragment of (a) which is capable of binding to RIP or inhibiting the NF- $\kappa$ B inducing effect of RIP;

(c) an analog of (a) or (b) which differs from the sequence of (a) or (b) by no more than 10 substitutions, deletions and/or insertions of amino acid residues and is capable of binding to RIP or inhibiting the NF- $\kappa$ B inducing effect of RIP.

14. A polypeptide according to claim 13, comprising a protein whose amino acid sequence is that of SEQ ID NO:2.

15. A polypeptide according to claim 13, which has the amino acid sequence of (b).

16. A pharmaceutical composition for the modulation of the RIP effect on cells, comprising, as active ingredient, the polypeptide according to claim 13.

17. A pharmaceutical composition for modulating the RIP effect on cells, comprising, as active ingredient, a recombinant animal virus vector encoding a protein capable of binding a cell surface receptor and encoding the RAP protein according to claim 13.

18. Antibodies or active fragments or derivatives thereof, specific for a polypeptide according to claim 13.

19. A method for modulating RIP modulated/mediated effect on cells, comprising treating said cells with antibodies or active fragments or derivatives thereof according to claim 18, said treating being by application of a suitable composition containing said antibodies, active

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fragments or derivatives thereof to said cells, wherein when the RAP protein or portions thereof of said cells are exposed on the extracellular surface, said composition is formulated for extracellular application, and when said RAP proteins are intracellular said composition is formulated for intracellular application.

20. A method for the modulation or mediation of the RIP modulated/mediated intracellular effects on the inflammation, cell death or cell survival pathways in which RIP is involved directly, or indirectly via other modulators/mediators of these pathways, comprising treating said cells with one or more polypeptides according to claim 13, capable of binding to RIP and modulating or mediating said intracellular activity of RIP, wherein said treating of said cells comprises introducing into said cells said one or more polypeptides in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more polypeptides in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

21. A method for the modulation of the RIP modulated/mediated effect on cells according to claim 20, wherein said treating of cells comprises introducing into said

cells a DNA sequence encoding said polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

22. A method according to claim 20, wherein said treating of said cells is by transfection of said cells with a recombinant animal virus vector comprising:

(a) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein (ligand) that is capable of binding to a specific cell surface receptor on the surface of said cells to be treated and a second sequence encoding said polypeptide, that when expressed in said cells is capable of modulating/mediating the activity of RIP; and

(b) infecting said cells with said vector of (a).

23. A method for treating tumor cells or HIV-infected cells or other diseased cells, comprising:

(a) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein capable of binding to a specific tumor cell surface receptor or HIV-infected cell surface receptor or receptor carried by other diseased cells and a sequence encoding a polypeptide of claim 13, that when expressed in said tumor, HIV-infected, or other diseased cell is capable of enhancing the RIP

modulated/mediated direct or indirect killing of said cell;  
and

(b) infecting said tumor or HIV-infected cells or other diseased cells with said vector of (a).

24. A method for modulating the RIP effect on cells, comprising applying the ribozyme procedure in which a vector encoding a ribozyme sequence capable of interacting with a cellular mRNA sequence encoding a polypeptide according to claim 13 is introduced into said cells in a form that permits expression of said ribozyme sequence in said cells, and wherein when said ribozyme sequence is expressed in said cells it interacts with said cellular mRNA sequence and cleaves said mRNA sequence resulting in the inhibition of expression of said polypeptide in said cells.

25. A method for isolating and identifying polypeptides according to claim 13, capable of binding directly to RIP, comprising applying the yeast two-hybrid procedure in which a sequence encoding said RIP is carried by one hybrid vector and sequence from a cDNA or genomic DNA library is carried by the second hybrid vector, the vectors then being used to transform yeast host cells and the positive transformed cells being isolated, followed by extraction of the said second hybrid vector to obtain a sequence encoding a polypeptide which binds to said RIP.

26. A method of modulating processes modulated/mediated by RIP directly or indirectly, comprising treating said cells with one or more polypeptide according to claim 13, capable of binding to RIP, wherein said treating of said cells comprises introducing into said cells said one or more polypeptide in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

27. A method of modulating processes that are mediated/modulated by RIP directly or indirectly and which include the inhibition of NF- $\kappa$ B and JNK, comprising treating said cells with one or more polypeptides according to claim 13 capable of binding to RIP, wherein said treating of cells comprises introducing into said cells said one or more polypeptides in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

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